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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------------|------------------------|
| 10/690,049 | 10/21/2003 | Tomohiro Kono | 038779/270668 | 3500 |
| 826 | 7590 | 09/19/2007 | | |
| ALSTON & BIRD LLP BANK OF AMERICA PLAZA 101 SOUTH TRYON STREET, SUITE 4000 CHARLOTTE, NC 28280-4000 | | | EXAMINER TON, THAIAN N | |
| | | | ART UNIT 1632 | PAPER NUMBER |
| | | | MAIL DATE 09/19/2007 | DELIVERY MODE PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/690,049

Applicant(s)

KONO ET AL.

Examiner

Thaia N. Ton

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-5 and 7-22 is/are pending in the application.
- 4a) Of the above claim(s) 7-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-5 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' Amendments and Remarks, filed 6/27/07, have been considered. Claims 3-5, 7-22 are pending; claims 7-21 are withdrawn; claims 3-5 and 22 are amended and under current examination.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on July 19, 2006 is acknowledged.

Claims 7-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/19/06.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

The objections to claims 5 and 22 is withdrawn. The Examiner notes that the objection to claim 5 should have been to claim 4, and Applicants have correctly amended claim 4 to recite "embryonic stem cell".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-5 and 22 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record, advanced in the Office action, mailed 3/27/07.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments. Applicants argue that the rejection based on the alleged deficiencies of Example 1 should be removed as a basis for any rejection against the pending claims. See page 7 of the Remarks. Applicants argue that the claims are now directed to utilizing embryonic stem cells, therefore, the examples detailing the use of mouse ES cells provide sufficient guidance to one skilled in the art to make and use the currently claimed invention without undue experimentation.

Response to Arguments. Applicants' arguments have been fully considered, but are not persuasive. Although the claims have now been amended to recite utilizing *embryonic stem cells*, the basis of the prior rejection is maintained for reasons of record.

In particular, it should be made clear that, the enabling specification must teach those skilled in the art to make and use the full scope of the claimed invention without undue experimentation. "Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue

experimentation." *Vaeck*, 947 F.2d at 495, 20 USPQ2d at 1444; *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404; *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification)." *In re Wright* (CAFC) 27 USPQ2d 1510 at 1513.

In the instant case, the breadth of the claims requires using any type of ES cells, from any species, electrically stimulating the ES cell and using a single antibody against a membrane antigen marker that is specifically expressed in undifferentiated cells, and synchronizing the undifferentiated cells. The full scope of these claims is not enabled as stated in the prior Office action.

Applicants' Arguments. Applicants argue that when conducting an experiment using ES cells, it is understood that there is possibility that some of the ES cells may be differentiated under various influences, to produce differentiated cells (such as those referred to in Comparative Example 2), cells that are differentiated from ES cells. Applicants argue that the coexistence of these differentiated cells have disadvantageous effects by lowering the efficiency of NT. Therefore, the technical features of the present invention resides in selecting undifferentiated cells only, to increase the effectiveness of donor cells for NT. See page 8 of the Response. Applicants argue that the independent claim has now been amended to clarify that the membrane antigen marker is "specifically expressed in undifferentiated ES cells" and claim 22 has been amended to only consist of SSEA-1 and sca-1, which are specifically expressed.

Response to Arguments. These arguments are not persuasive, because although a marker may be expressed in ES cells, it could also be expressed in other cell types (as evidenced by the art of Pera, Ling and Went, cited the prior rejection of record). A specifically expressed marker is one that would uniquely identify a population of cells. The Examiner cites Lee *et al.* (Chest: 114(6): 1542-1545, 1998) as further evidence that although SSEA-1 is expressed in murine embryos, and

mouse ES cells, it is also expressed in embryonal carcinoma cells and human granulocytes (see p. 1542, 2nd col, 1st ¶). Similarly, the NIH ("Appendix E: Stem Cell Markers", pages 1-8 accessed online at <http://stemcells.nih.gov/info/scireport/appendixe.asp#eii>, Sept. 5, 2007, publicly available June 17, 2001) that states that Sca-1 (stem cell antigen) is expressed in hematopoietic stem cells and mesenchymal stem cells (see page 5). Given that Applicants' have stated that the advantage of their invention is to separate differentiated cells from undifferentiated ES cells, and that culture conditions can cause differentiation of ES cells, utilizing Applicants' invention, wherein only one antibody against a membrane antigen marker is used to separate the cells, it would have required undue experimentation for one of skill in the art to determine if the resultant cells are undifferentiated ES cells, or cells that are now differentiated that express a common marker as an ES cell. For example, with regard to claim 22, the expression of sca-1 or SSEA-1 would not necessarily result in isolation of ES cells, because the ES cells used in the methods could have differentiated into other cell types that express these markers.

Applicants' Arguments. Applicants argue that the specification and working examples need not disclose every possible permutation or embodiment of the currently claimed invention, as long as the application adequately represents the claimed invention. Thus, Applicants argue that because the working examples detail the use of mouse ES cells in one embodiment, the specific examples exemplify selection of undifferentiated ES cells using SSEA-1, which is an appropriate marker for a mouse ES cell. Applicants argue that, "Since the membrane antigen markers that are specifically expressed in undifferentiated embryonic stem cells from various species are well known in the relevant art, one skilled in the art easily knows the marker that is specifically expressed in the specific ES cells being used and can equally easily select a proper antibody against the marker. For instance, one example is the use of an antigen against SSEA-1 when working with mouse ES

cells (example 2). In light of the knowledge of one skilled in the art coupled with the details set forth in the application, one skilled in the art can readily practice the currently claimed invention without undue experimentation.”

Response to Arguments. These arguments have been considered, but are not persuasive. The claims recite utilizing “embryonic stem cells”, there is no indication that the embryonic stem cells used in step (a) of the claims are all isolated from the same species. Thus, this could encompass a population of ES cells, which are derived from different species. Although Applicants are not required to disclose every possible permutation or embodiment of a claimed invention, the claimed invention must be enabled for its full scope. In the instant case, the term “ES cells” encompasses cells from any species, or even mixtures and combinations of ES cells. As stated in the prior Office action, a specific marker, although expressed in an ES cell, can also be expressed in different cell types. The Examiner previously provided the NIH definition for an ES cell, which clearly shows that these cells have specific, art-recognized characteristics, which include specific markers, but those markers, by themselves do not necessarily define an ES cell. Thus, the instantly claimed method is not enabled, because step (b) recites selecting for undifferentiated ES cells utilizing a marker “specifically expressed” in undifferentiated ES cells. The working examples utilizing SSEA-1 as a marker to select for undifferentiated ES cells. However, as shown by the art of Lee (above), SSEA-1 is expressed in cells other than mouse ES cells, for example, in embryonal carcinoma cells and human granulocytes. Additionally, the breadth of the claims is directed to any marker that is specifically expressed in undifferentiated ES cells. However, the various markers contemplated by the specification fail to provide specific guidance as to how to specifically and uniquely isolate an undifferentiated cell from a heterogeneous population of cells, because these markers are expressed (or not expressed) variably in different species (such as between mouse and human ES cells), as well as in different cell types (such as ES cells and hematopoietic stem

cells. Accordingly, one of skill in the art, given the limited teachings in the specification, would not be able to practice the claimed invention without undue experimentation, because one of skill would not be able to uniquely identify undifferentiated cells to practice the claimed invention.

Claim Rejections - 35 USC § 112

The prior rejection of claims 3, 5, and 22 is withdrawn in view of Applicants' amendments to the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is incomplete. This is a new ground of rejection, necessitated by Applicants' amendment to the claim. The metes and bounds of the claim are indefinite, because the preamble of the method steps of the claim fails to relate to the preamble, "A method for preparing donor cells for nuclear transfer." Specifically, the method steps relate to embryonic stem cells, and do not relate to donor cells. Thus, the preamble is broader than the method steps, which require a specific type of cell. Appropriate correction is required. Claims 4, 5 and 22 depend from claim 3.

Art Unit: 1632

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Thaian N. Ton/
Primary Examiner
Art Unit 1632